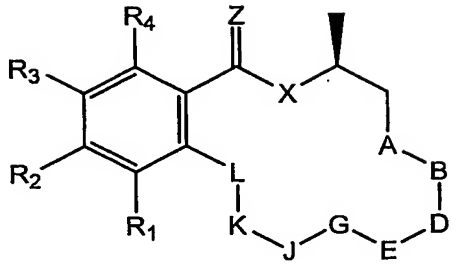
CLAIMS

What is claimed is:

1. A compound having the structure:



wherein

R_1 is hydrogen, halogen, cyano, $-OR_A$, $-N(R_A)_2$, $-SR_A$, $-O(C=O)R_A$, $-N(R_A)(C=O)(R_A)$, $-C(O)R_A$, $-C(O)OR_A$, $-CON(R_A)_2$, $-OCO_2R_A$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_A is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

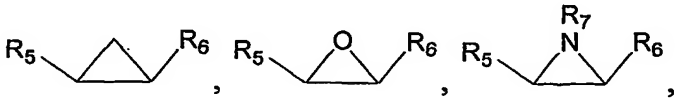
R_2 is hydrogen, halogen, cyano, $-OR_B$, $-N(R_B)_2$, $-SR_B$, $-O(C=O)R_B$, $-N(R_B)(C=O)(R_B)$, $-C(O)R_B$, $-C(O)OR_B$, $-CON(R_B)_2$, $-OCO_2R_B$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_3 is hydrogen, halogen, cyano, $-OR_C$, $-N(R_C)_2$, $-SR_C$, $-O(C=O)R_C$, $-N(R_C)(C=O)(R_C)$, $-C(O)R_C$, $-C(O)OR_C$, $-CON(R_C)_2$, $-OCO_2R_C$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_C is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

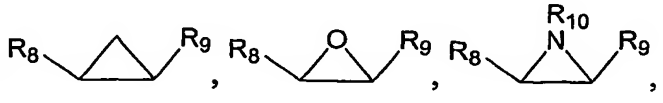
R_4 is hydrogen, halogen, cyano, $-OR_D$, $-N(R_D)_2$, $-SR_D$, $-O(C=O)R_D$, $-N(R_D)(C=O)(R_D)$, $-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, $-OCO_2R_D$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

Z is O, S, or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

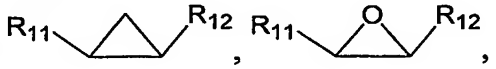
A and B together represent 

$-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

D and E together represent 

$-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

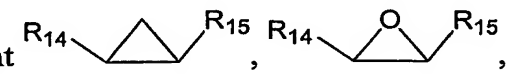
$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{10} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_8-CHR_9-$, R_9 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

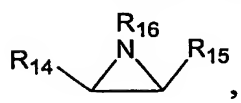
G and J together represent  , ,

 ,

$-CHR_{11}-CHR_{12}-$, $-CR_{11}=CR_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{13} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{11}-CHR_{12}-$, R_{11} and R_{12} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

K and L together represent  , ,

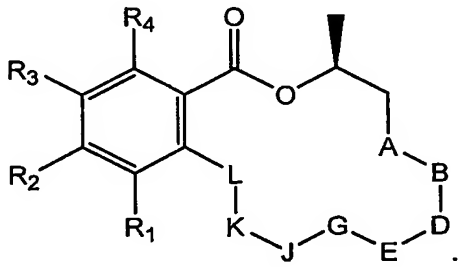
 ,

$-CHR_{14}-CHR_{15}-$, $-CR_{14}=CR_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{16} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{14}-CHR_{15}-$, R_{14} and R_{15} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

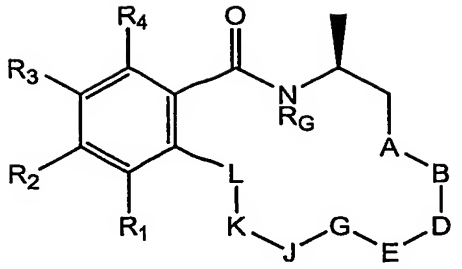
whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted; and

pharmaceutically acceptable derivatives thereof.

2. The compound of claim 1, wherein Z and X are each O, and the compound has the structure:

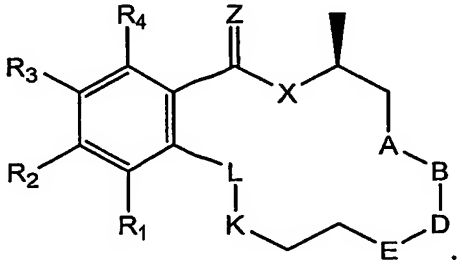


3. The compound of claim 1, wherein Z is O and X is NR_G, and the compound has the structure:

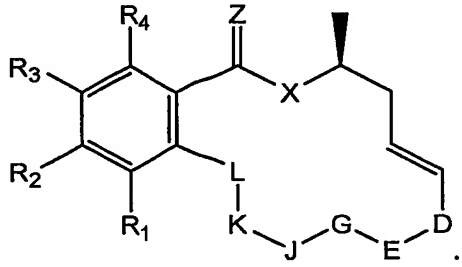


4. The compound of claim 3, wherein R_G is H.

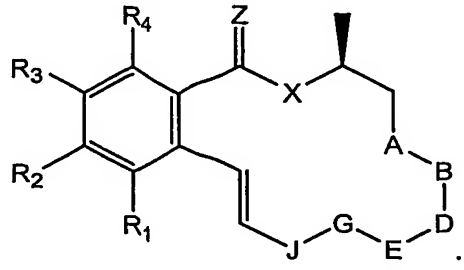
5. The compound of claim 1, wherein G and J together represent $-CH_2-CH_2-$ and the compound has the structure:



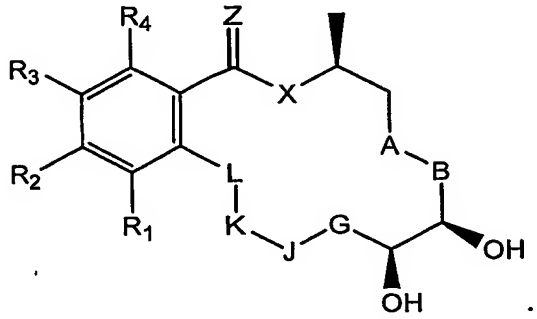
6. The compound of claim 1, wherein A-B is –CH=CH- and the compound has the structure:



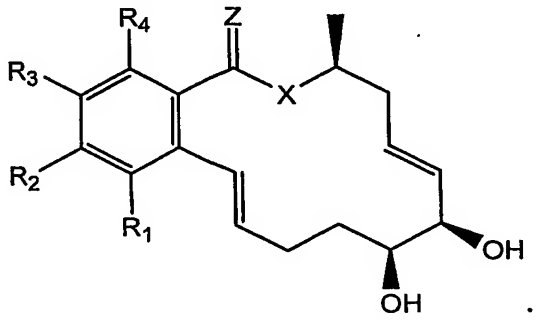
7. The compound of claim 1, wherein K and L together represent –CH=CH- and the compound has the structure:



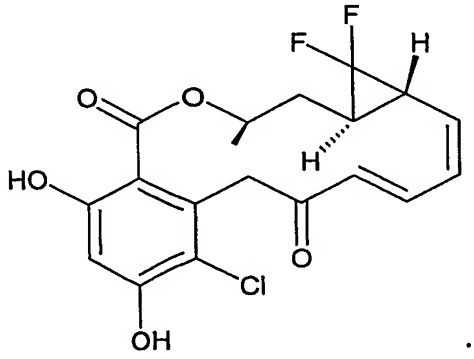
8. The compound of claim 1, wherein D and E together represent -CHOH=CHOH- and the compound has the structure:



9. The compound of claim 1, wherein A, B, D, E, G, J, K, and L are as represented in the structure:



10. A compound of structure:



11. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11, further comprising one or more additional therapeutic agents.

13. The pharmaceutical composition of claim 12, wherein the one or more additional therapeutic agents comprises an anticancer agent.

14. A method for treating cancer comprising:

administering a therapeutically effective amount of a compound of claim 1 to a subject in need thereof.

15. The method of claim 14, wherein the therapeutically effective amount is in the range of 0.001 mg/kg to 50 mg/kg of body weight.

16. The method of claim 14, wherein the therapeutically effective amount is in the range of 0.01 mg/kg to about 25 mg/kg of body weight.

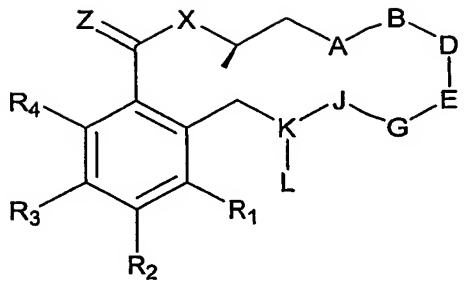
17. The method of claim 14, said method further comprising administering one or more additional therapeutic agents in combination with the compound.

18. The method of claim 17, wherein the one or more additional therapeutic agents comprises an anticancer agent.

19. A method for inhibiting the growth of or killing cancer cells, said method comprising:

contacting the cancer cells with an amount of a compound of claim 1 effective to inhibit the growth of or kill cancer cells.

20. A method for the synthesis of a compound having the structure (I):



(I)

wherein

R_1 is hydrogen, halogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or $N(R_A)_2$, wherein each occurrence of R_A is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

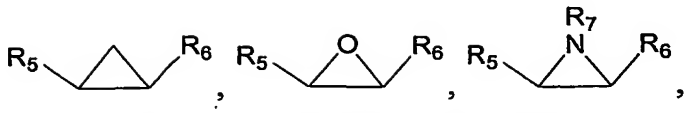
R_2 is hydrogen, halogen, cyano, $-OR_B$, $-N(R_B)_2$, $-SR_B$, $-O(C=O)R_B$, $-N(R_B)(C=O)(R_B)$,
$-C(O)R_B$, $-C(O)OR_B$, $-CON(R_B)_2$, $-OCO_2R_B$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_3 is hydrogen, halogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or $-N(R_C)_2$, wherein each occurrence of R_C is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_4 is hydrogen, halogen, cyano, $-OR_D$, $-N(R_D)_2$, $-SR_D$, $-O(C=O)R_D$, $-N(R_D)(C=O)(R_D)$,
$-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, $-OCO_2R_D$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent  ,

$-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

D and E together represent $-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen or lower alkyl;

G and J together represent $-CHR_{10}-CHR_{11}-$, $-CR_{10}=CR_{11}-$, wherein R_{10} and R_{11} are each independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, $CH-CH_3$, $CH-CH(R_L)_2$, $C=C(R_L)_2$, $-CH_2-$,

$-C(-S(CH_2)_3S-)-$, $CH-OR_L$, $CH-SR_L$, $CH-N(R_L)_2$, $CH-N(R_L)(C=O)(R_L)$, $C=N-O-R_L$, $CH-N=O$, $C=C(R_L)-N(R_L)_2$, $C=N-R_L$, $C=N-N(R_L)_2$, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent $C-N(R_L)_2$, wherein each occurrence of R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

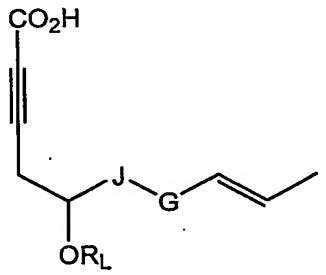
whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or

unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;

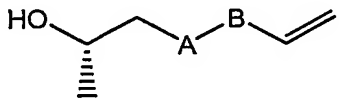
wherein one or any two of R_1, R_A, R_2, R_B, R_3, R_C, R_4, R_D, R_5, R_6, R_J, or R_L are optionally a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids,

said method comprising:

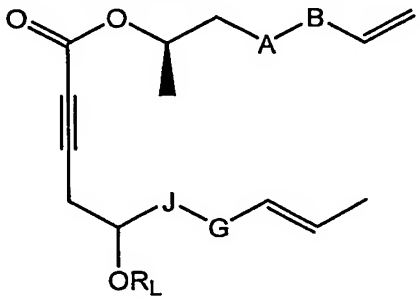
(1) reacting an acidic component having the structure:



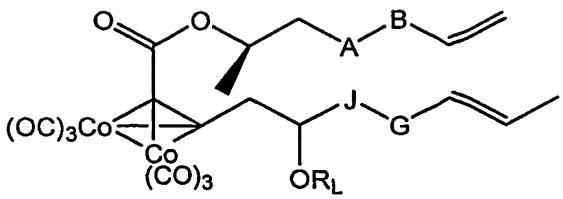
wherein R_L, J, and G are as defined above, with a chiral component having the structure:



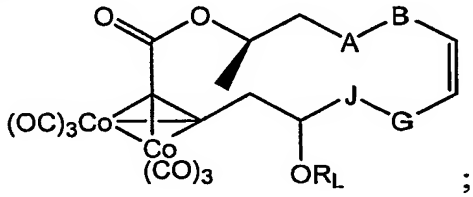
wherein A and B are as defined above, in the presence of an esterification reagent to generate an intermediate having the structure:



(2) complexing the intermediate with a cobalt, such as dicobalt hexcarbonyl, to yield a structure:



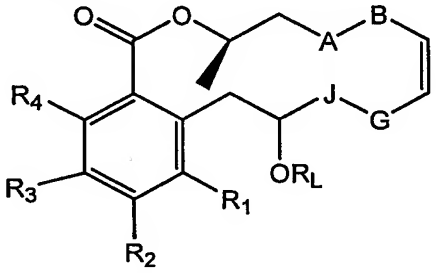
(3) cyclizing the combalt complex in the presence of an olefin metathesis catalyst to generate the compound:



;

(4) removing the cobalt to form a ynolide;

(5) reacting the alkyne moiety of the ynolide with a diene under cyclcoaddition conditions to generate the compound:



; and

(6) optionally further reacting the macrocycle with one or more reagents to diversify and optionally deprotecting the macrocycle to generate a compound having the formula (I).

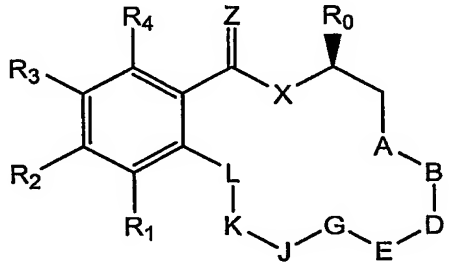
21. The method of claim 20, wherein the step of esterification is performed using diethylazodicarboxylate (DIAD) in the presence of triphenylphosphine or trifurylphosphine.

22. The method of claim 20, wherein the step of olefin metathesis is performed using an olefin metathesis catalyst.

23. The method of claim 20, wherein the step of olefin metathesis is performed using a ruthenium-based olefin metathesis catalyst.

24. The method of claim 23, wherein the step of olefin metathesis is performed using Ru(1,3-dimesityl-4,5-dihydro-imidazol-2-ylidene)(=CHCH=C(CH_3)$_2$)PCp_3Cl_2.

25. A method for synthesis of a macrocycle having the structure **(IIa)**:



(IIa)

wherein

R_0 is hydrogen, halogen, cyano, -OR_Z, -$N(R_Z)_2$, -SR_Z, -$O(C{=}O)R_Z$, -$N(R_Z)(C{=}O)(R_Z)$, -$C(O)R_Z$, -$C(O)OR_Z$, -$CON(R_Z)_2$, -OCO_2R_Z, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_Z is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety

R_1 is hydrogen, halogen, cyano, -OR_A, -$N(R_A)_2$, -SR_A, -$O(C{=}O)R_A$, -$N(R_A)(C{=}O)(R_A)$,
-$C(O)R_A$, -$C(O)OR_A$, -$CON(R_A)_2$, -OCO_2R_A, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_A is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_2 is hydrogen, halogen, cyano, -OR_B, -$N(R_B)_2$, -SR_B, -$O(C{=}O)R_B$, -$N(R_B)(C{=}O)(R_B)$,
-$C(O)R_B$, -$C(O)OR_B$, -$CON(R_B)_2$, -OCO_2R_B, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

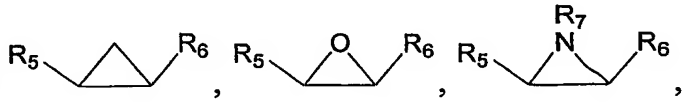
R_3 is hydrogen, halogen, cyano, -OR_C, -$N(R_C)_2$, -SR_C, -$O(C{=}O)R_C$, -$N(R_C)(C{=}O)(R_C)$,

$-C(O)R_C$, $-C(O)OR_C$, $-CON(R_C)_2$, $-OCO_2R_C$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_C is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

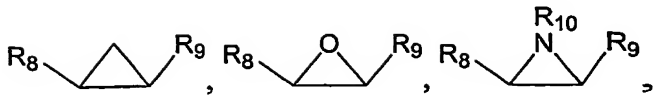
R_4 is hydrogen, halogen, cyano, $-OR_D$, $-N(R_D)_2$, $-SR_D$, $-O(C=O)R_D$, $-N(R_D)(C=O)(R_D)$, $-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, $-OCO_2R_D$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

Z is O, S, or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

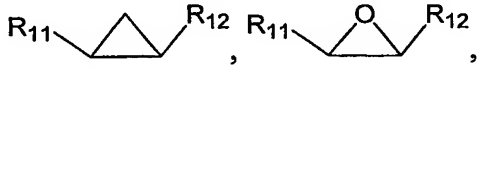
X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

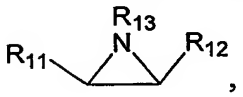
A and B together represent 

, $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

D and E together represent  ,

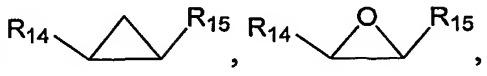
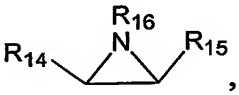
$-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{10} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_8-CHR_9-$, R_9 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

G and J together represent  ,

 ,

$-CHR_{11}-CHR_{12}-$, $-CR_{11}=CR_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{13} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{11}-CHR_{12}-$, R_{11}

and R_{12} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

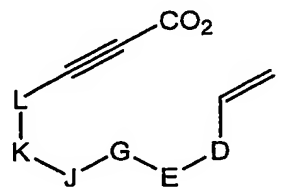
K and L together represent  ,  ,

$-CHR_{14}-CHR_{15}-$, $-CR_{14}=CR_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{16} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{14}-CHR_{15}-$, R_{14} and R_{15} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

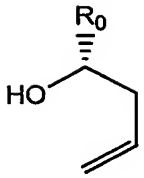
whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted,

said method comprising:

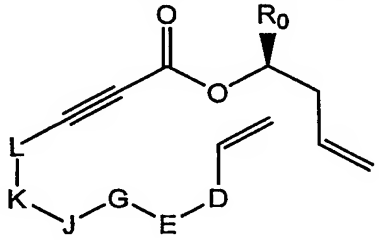
(1) reacting a component having the structure:



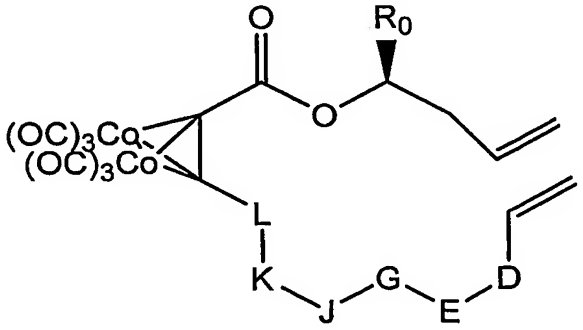
wherein R_L, J, and G are as defined above, with a chiral component having the structure:



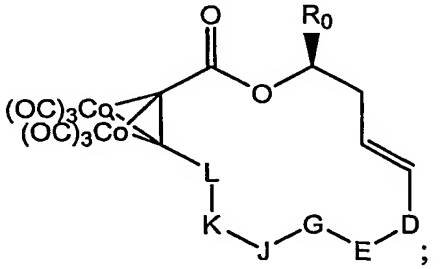
wherein A, B, D, E, G, J, K, and L are as defined above, in the presence of an esterification reagent to generate an intermediate having the structure:



(2) complexing the intermediate with a cobalt, such as dicobalt hexcarbonyl, to yield a structure:

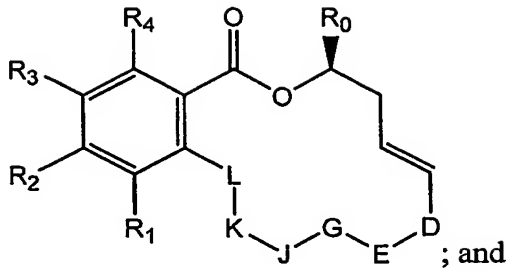


(3) cyclizing the combalt complex in the presence of an olefin metathesis catalyst to generate the compound:



(4) removing the cobalt to form a ynolide;

(5) reacting the alkyne moiety of the ynolide with a diene under cyclcoaddition conditions to generate the compound:



; and

(6) optionally further reacting the macrocycle with one or more reagents to diversify and optionally deprotecting the macrocycle to generate a compound having the formula (**IIa**).

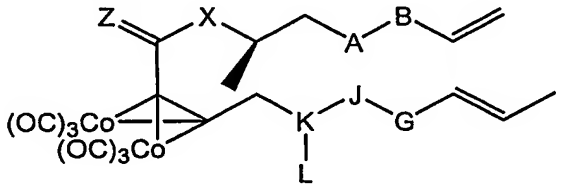
26. The method of claim 25, wherein the method further comprises further diversifying the macrocycle to generate a compound having the structure (**II**) as defined herein.

27. The method of claim 25, wherein the step of olefin metathesis is performed using an olefin metathesis catalyst.

28. The method of claim 25, wherein the step of olefin metathesis is performed using a ruthenium-based olefin metathesis catalyst.

29. The method of claim 28, wherein the step of olefin metathesis is performed using Ru(1,3-dimesityl-4,5-dihydro-imidazol-2-ylidene)(=CHCH=$C(CH_3)_2$)PCp_3Cl_2.

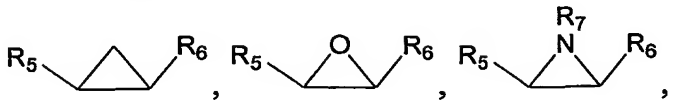
30. A compound of the formula:



wherein

Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent  , -CHR_5-CHR_6-, -CR_5=CR_6-, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, -OR_J, -$N(R_J)_2$, -SR_J, -O(C=O)R_J, -O(S=O)R_J ,-$N(R_J)$(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
-$CON(R_J)_2$, -OCO_2R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -$S(O)_2R_K$, -O(C=O)R_K, -$N(R_K)$(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -$CON(R_K)_2$, -OCO_2R_K, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR_5-CHR_6-, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring,

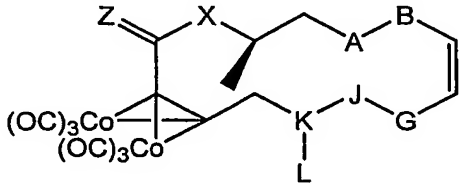
G and J together represent -CHR_{10}-CHR_{11}-, -CR_{10}=CR_{11}-, wherein R_{10} and R_{11} are each independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, CH-CH_3, CH-$CH(R_L)_2$, $C=C(R_L)_2$, -CH_2-, -C(-$S(CH_2)_3S$-)-, CH-OR_L, CH-SR_L, CH-$N(R_L)_2$, CH-$N(R_L)$(C=O)(R_L), C=N-O-R_L, CH-N=O, $C=C(R_L)$-$N(R_L)_2$, C=N-R_L, C=N-$N(R_L)_2$, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent C-$N(R_L)_2$, wherein each occurrence of R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;

wherein one or any two of R_A, R_B, R_C, R_D, R_5, R_6, R_J, or R_L are optionally a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids.

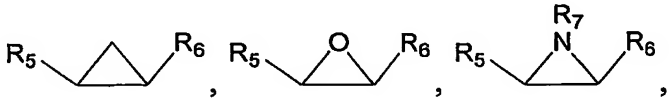
31. A compound of the formula:



wherein

Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent 

, $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring,

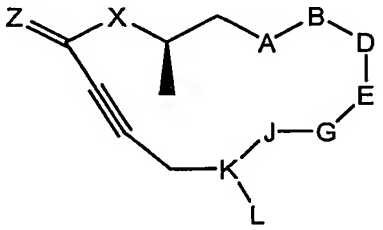
G and J together represent -CHR_{10}-CHR_{11}-, -CR_{10}=CR_{11}-, wherein R_{10} and R_{11} are each independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, CH-CH_3, CH-$CH(R_L)_2$, $C=C(R_L)_2$, -CH_2-, -$C(-S(CH_2)_3S-)$-, CH-OR_L, CH-SR_L, CH-$N(R_L)_2$, CH-$N(R_L)(C=O)(R_L)$, C=N-O-R_L, CH-N=O, $C=C(R_L)$-$N(R_L)_2$, C=N-R_L, C=N-$N(R_L)_2$, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent C-$N(R_L)_2$, wherein each occurrence of R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;

wherein one or any two of R_A, R_B, R_C, R_D, R_5, R_6, R_J, or R_L are optionally a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids.

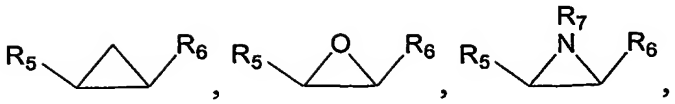
32. A compound of the formula:



wherein

Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent  , -CHR_5-CHR_6-, -CR_5=CR_6-, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, -OR_J, -$N(R_J)_2$, -SR_J, -$O(C=O)R_J$, -$O(S=O)R_J$,-$N(R_J)(C=O)(R_J)$, -$C(=O)R_J$, -$C(=O)OR_J$,

-$CON(R_J)_2$, -OCO_2R_J, -$OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, -OR_K, -SR_K, -$C(O)OR_K$, -$C(O)NR_K$, -$S(O)_2R_K$, -$O(C=O)R_K$, -$N(R_K)(C=O)(R_K)$, -$C(O)R_K$, -$C(O)OR_K$, -$CON(R_K)_2$, -OCO_2R_K, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR_5-CHR_6-, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

D and E together represent -CHR_8-CHR_9-, -CR_8=CR_9-, wherein R_8 and R_9 are each independently hydrogen or lower alkyl;

G and J together represent -CHR_{10}-CHR_{11}-, -CR_{10}=CR_{11}-, wherein R_{10} and R_{11} are each independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, CH-CH_3, CH-$CH(R_L)_2$, C=$C(R_L)_2$, -CH_2-,

-$C(-S(CH_2)_3S-)$-, CH-OR_L, CH-SR_L, CH-$N(R_L)_2$, CH-$N(R_L)(C=O)(R_L)$, C=N-O-R_L, CH-N=O, C=$C(R_L)$-$N(R_L)_2$, C=N-R_L, C=N-$N(R_L)_2$, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent C-$N(R_L)_2$, wherein each occurrence of R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

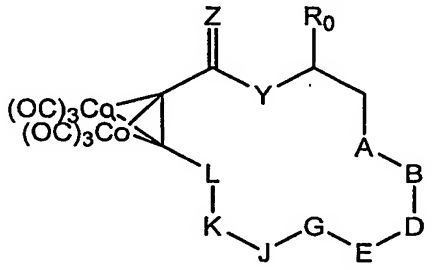
whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or

unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;

wherein one or any two of R_A, R_B, R_C, R_D, R_5, R_6, R_J, or R_L are optionally a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids.

33. The compound of claim 32, wherein D and E together represent $-CR_8=CR_9-$.

34. A compound of formula:

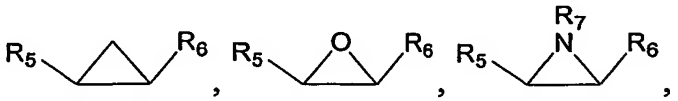


wherein

R_0 is hydrogen, cyano, $-OR_Z$, $-N(R_Z)_2$, $-SR_Z$, $-O(C=O)R_Z$, $-N(R_Z)(C=O)(R_Z)$, $-C(O)R_Z$, $-C(O)OR_Z$, $-CON(R_Z)_2$, $-OCO_2R_Z$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_Z is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety

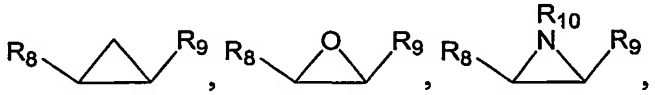
Z is O, S, or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent 

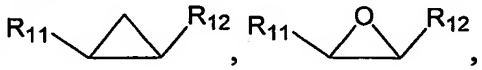
, $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

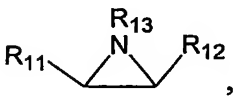
$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

D and E together represent  ,

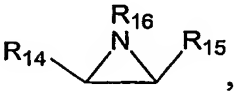
$-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{10} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_8-CHR_9-$, R_9 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

G and J together represent  ,

 ,

$-CHR_{11}-CHR_{12}-$, $-CR_{11}=CR_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{13} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{11}-CHR_{12}-$, R_{11} and R_{12} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

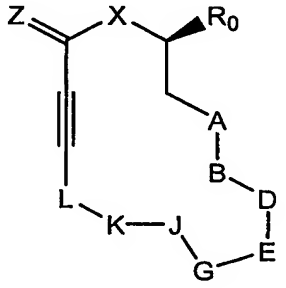
K and L together represent  ,  ,
 ,

$-CHR_{14}-CHR_{15}-$, $-CR_{14}=CR_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{16} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{14}-CHR_{15}-$, R_{14} and R_{15} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted.

35. The compound of claim 34, wherein A and B together represent $-CR_5=CR_6-$.

36. A compound of the formula:

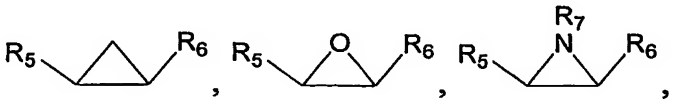


wherein

R_0 is hydrogen, cyano, $-OR_Z$, $-N(R_Z)_2$, $-SR_Z$, $-O(C=O)R_Z$, $-N(R_Z)(C=O)(R_Z)$, $-C(O)R_Z$, $-C(O)OR_Z$, $-CON(R_Z)_2$, $-OCO_2R_Z$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_Z is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety

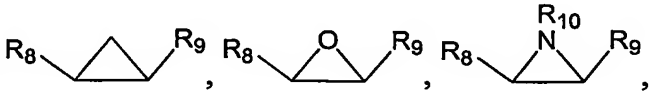
Z is O, S, or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent 

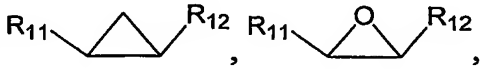
, $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently

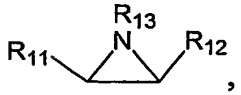
hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

D and E together represent  ,

$-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

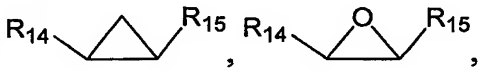
$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{10} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_8-CHR_9-$, R_9 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

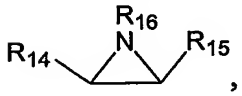
G and J together represent  ,

 ,

$-CHR_{11}-CHR_{12}-$, $-CR_{11}=CR_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{13} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{11}-CHR_{12}-$, R_{11} and R_{12} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

K and L together represent  , ,

 ,

$-CHR_{14}-CHR_{15}-$, $-CR_{14}=CR_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,

$-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_{16} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{14}-CHR_{15}-$, R_{14} and R_{15} taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring;

whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted.

37. The compound of claim 36, wherein A and B together represent $-CR_5=CR_6-$.

38. The compoud of claim 36, wherein the compound has the formula: